DT04 Rec'd PCT/PTO 0 8 OCT 2004

IN THE CLAIMS:

1. (Original) Use for the preparation of disease-modifying drugs drugs for the prevention and treatment of arthritis therapy of compounds or salts thereof having the following general formula:

$$A\text{-}(B)_{b0}\text{-}(C)_{c0}\text{-}N(O)_S \qquad (I)$$

wherein:

s is an integer and is equal to 1 or 2, preferably 2;

c0 is an integer and is equal to 0 or 1;

b0 is an integer and is 0 or 1; with the proviso that at least one between c0 and b0 is different from zero;

A = R-T_1-, wherein

R- is the radical of a non steroidal antiinflammatory precursor drug excluding the compounds having 2-oxo-1H-indolic structure, or the radical of a non steroidal antiinflammatory/analgesic drug;

T_1 = $(CO)_t$ or $(X)_{t'}$, wherein X = -O-, -S-, -N(R_{1C})-, R_{1C} is H or C_1-C_5 linear or branched alkyl, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1;

B = -T_B-X_2-T_{BI}- wherein

T_B and T_{BI} are equal or different;

T_B= (CO) when the reactive function in the precursor drug is -OH or –NH(R_{1C}); T_B = X, as above, when the reactive function in the precursor drug is -COOH;

T_{BI} = $(CO)_{tx}$ or $(X)_{txx}$, wherein tx and txx have the value of 0 or 1; with the proviso that tx = 1 when txx = 0, tx = 0 when txx = 1; X is as above;

X_2 is a bivalent linking group as defined below;

C is the bivalent radical -T_c-Y- wherein

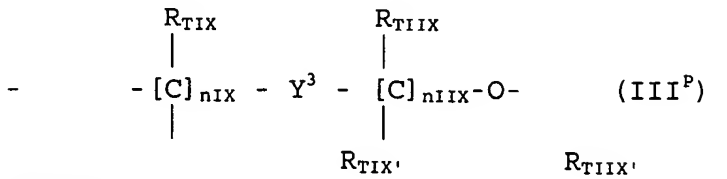
when b0 = c0 = 1: T_C = (CO) when tx = 0, T_C = X when txx = 0, X being as above;

when b0 = 0: T_C = (CO) when t = 0, T_C = X when t' = 0, X being as above;

when c0 = 0: tx = 0, T_{BI} = X = -O-.

Y is:

Y_p:



(III^P)

wherein:

nIX is an integer from 0 to 10, preferably from 1 to 3;

nIIX is an integer from 1 to 10, preferably from 1 to 3;

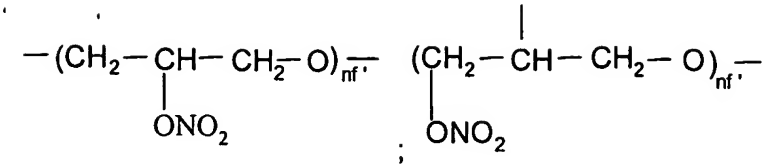
R_{TIX}, $R_{TIX'}$, R_{TIIX}, $R_{TIIX'}$, equal to or different from each other are H or C_1-C_4 linear or branched alkyl; preferably R_{TIX}, $R_{TIX'}$, R_{TIIX}, $R_{TIIX'}$ are H.

Y^3 is a saturated, unsaturated or aromatic heterocyclic ring containing one or two nitrogen atoms having 5 or 6 atoms,

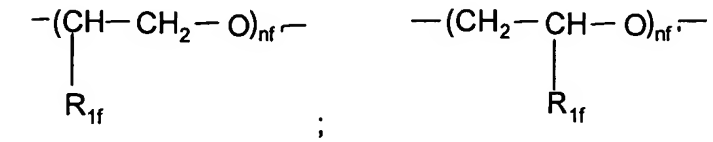
or Y can be:

Y_0, selected from the following:

- a –R'O– alkylenoxy group wherein R' is linear or branched when possible C_1-C_{20}, preferably having from 2 to 6 carbon atoms, or a cycloalkylene having from 5 to 7 carbon atoms, in the cycloalkylene ring one or more carbon atoms can be substituted by heteroatoms, the ring can have side chains of R' type, R' being as above; or one of the following groups:

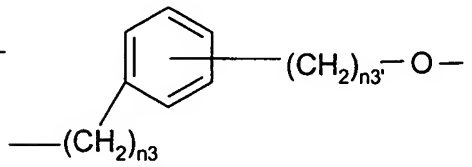
- 

wherein nf' is an integer from 1 to 6 preferably from 1 to 4;

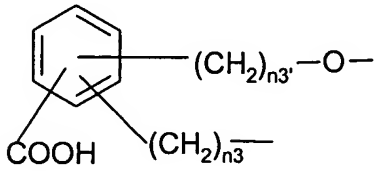
- 

wherein R_{1f} = H, CH_3 and nf' is an integer from 1 to 6; preferably from 1 to 4;

or Y is Y_{Ar} and is selected from the following:

- 

wherein n3 is an integer from 0 to 3 and n3' is an integer from 1 to 3;

- 

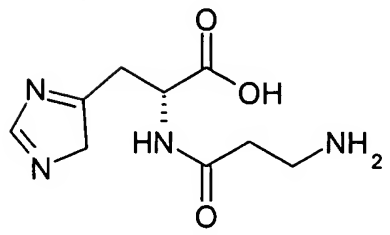
wherein n3 and n3' have the above meaning;

X_2, bivalent radicalm is such that the corresponding precursor of B, -T_B-X_2-T_{BI}- wherein the free valences of T_B and of T_{BI} are saturated each with OZ, with Z or with -N(Z^I)(Z^{II}), wherein Z = H, C_1-C_{10}, preferably C_1-C_5 linear or branched when possible alkyl, Z^I, Z^{II} equal or different have the Z values as above, depending on that T_B and/or T_{BI} = CO or X, in function of the values of t, t', tx and txx;

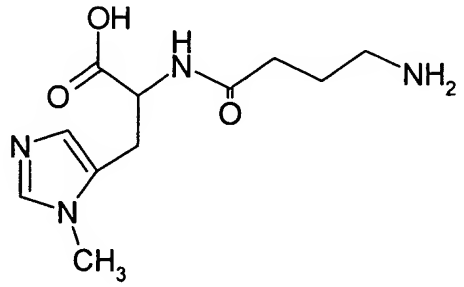
the precursor of B is selected from the following:

- aminoacids,
- hydroxyacids,
- aromatic and heterocyclic mono- and polyalchols,
- compounds containing at least one free acid function.

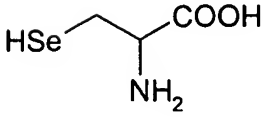
2. (Original) Use according to claim 1, wherein the precursor of B is selected from the following: - aminoacids selected from the following: L-carnosine (formula CI), anserine (CII), selenocysteine (CIII), selenomethionine (CIV), penicillamine (CV), N-acetylpenicillamine (CVI), cysteine (CVII), N-acetylcysteine (CVIII), glutathione (CIX) or esters thereof, preferably ethyl or isopropyl ester:



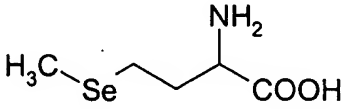
(CI)



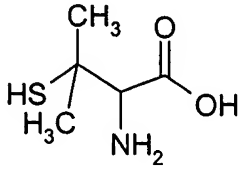
(CII)



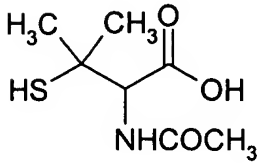
(CIII)



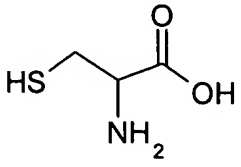
(CIV)



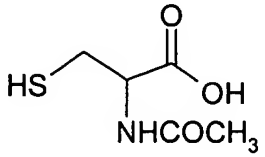
(CV)



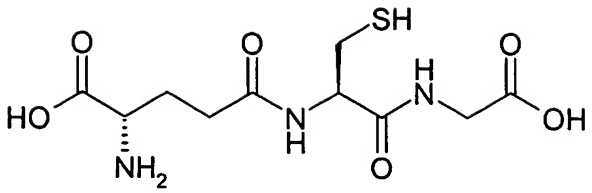
(CVI)



(CVII)

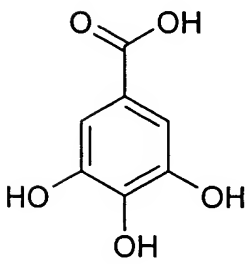


(CVIII)

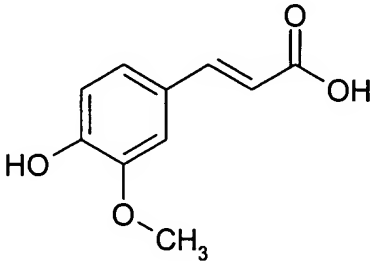


(CIX)

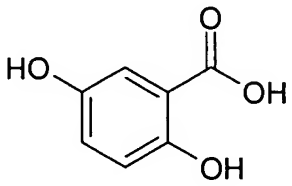
- hydroxyacids, selected from the following: gallic acid (formula DI), ferulic acid (DII), gentisic acid (DIII), citric acid (DIV), caffeic acid (DV), dihydrocaffeic acid (DVI), p-cumaric acid (DVII), vanillic acid (DVIII):



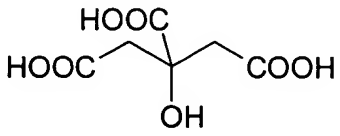
(DI)



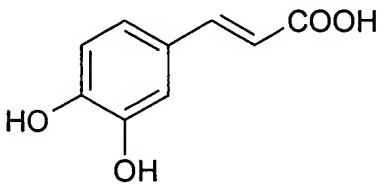
(DII)



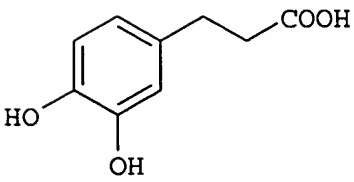
(DIII)



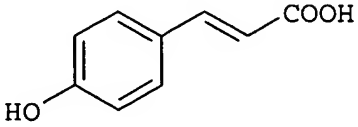
(DIV)



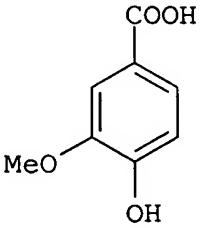
(DV)



(DVI)



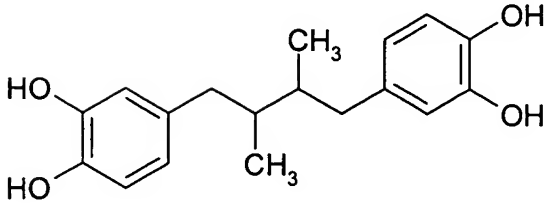
(DVII)



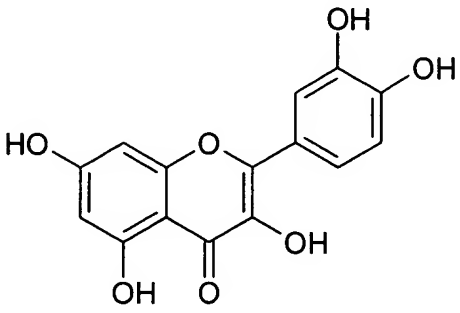
(DVIII)

- aromatic and heterocyclic mono- and polyalcohols, selected from the following: nordihydroguaiaretic acid (EI), quercetin (EII), catekin

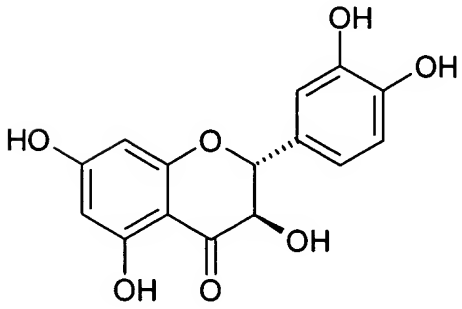
(EIII), kaempferol (EIV), sulphurethyne (EV), hydroquinone (EVIII), gossypol (EIX), reductic acid (EX), methoxyhydroquinone (EXI), hydroxyhydroquinone (EXII), propyl gallate (EXIII), 3,5-di-ter-butyl-4-hydroxybenzyl-thioglycolate (EXXIV), allopurinol (EXXXI); saccharose (EC), ascorbic (ECI) and isoascorbic acid (ECII), p-cumaric alcohol (ECIII), 4-hydroxy-phenylethylalcohol (ECIV), coniferyl alcohol (ECV):



(EI)



(EII)



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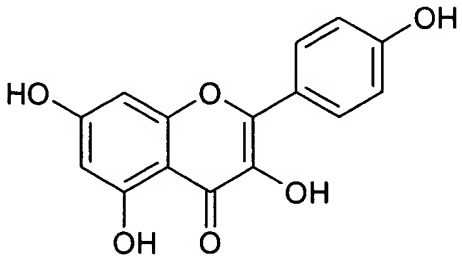
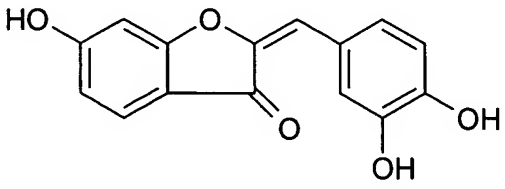
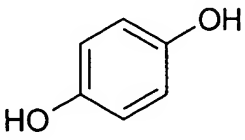


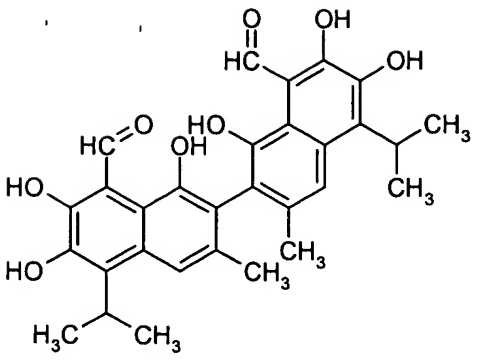
(EIV)



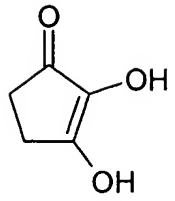
(EV)



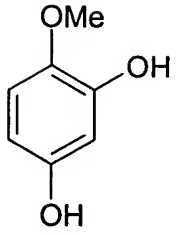
(EVIII)



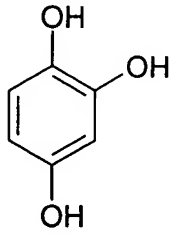
(EIX)



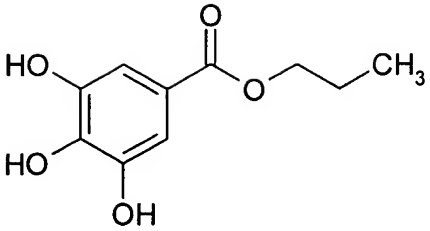
(EX)



(EXI)



(EXII)



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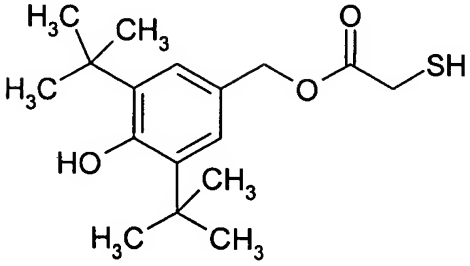
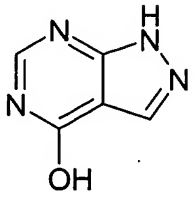
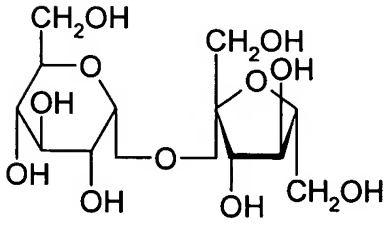


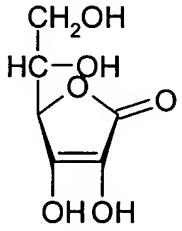
(EXXIV)



(EXXXI)



(EC)



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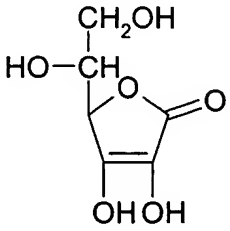
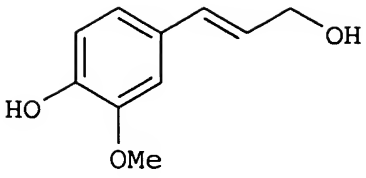


(ECII)



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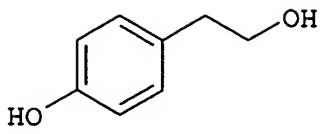
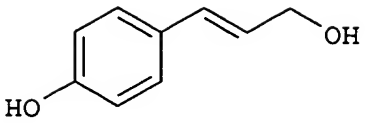
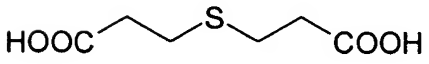


(ECIV)

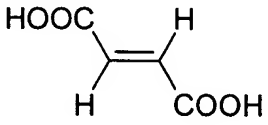


(ECV)

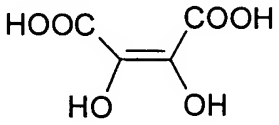
- compounds containing at least one free acid function, selected from the following: 3,3'-thiodipropionic acid (NI), fumaric acid (NII), dihydroxymaleic acid (NIII), edetic acid (NV):



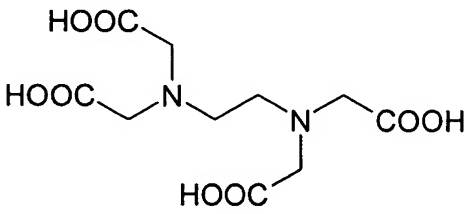
(NI)



(NII)



(NIII)



(NV)

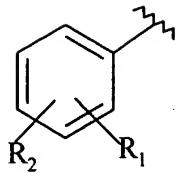
3. (Currently Amended) Use according to claims 1-~~2~~, wherein in the compounds of formula (I) when b0 = c0 = 1, the bonds between the drug radical and X_2 and between X_2 and Y are, independently the one from the other, of ester, thioester, amide type;

when b0 = 0 and c0 = 1 the bond between the drug radical and Y is of ester, thioester, amide type.

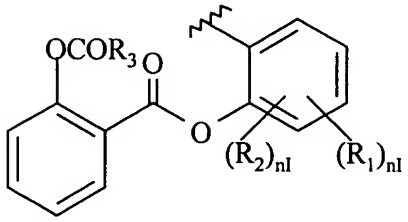
4. (Currently Amended) Use according to claims 1-~~3~~, wherein the R radical is selected from the following groups:

Group I)

Ia)



Ib)



wherein:

R_1 is H or -$OCOR_3$; wherein R_3 is methyl, ethyl or C_3-C_5 linear or branched alkyl, or the residue of an heterocycle with only one ring having 5 or 6 atoms partially or totally hydrogenated, or aromatic, containing one or more heteroatoms independently selected from O, N and S;

R_2 is hydrogen, hydroxy, halogen, C_1-C_4 linear or branched alkyl, C_1-C_4 linear or branched alkoxyl; a C_1-C_4 linear or branched perluoroalkyl, for example trifluoromethyl; nitro, amino, mono- or di-(C_{1-4}) alkylamino;

with the proviso that in formula Ia) R_1 and R_2 are not contemporaneously H;

preferably when R_1 = H R_2 = OH;

preferably in the compounds of formula Ia) T_1 = -CO- and:

- R_1 = acetoxy, preferably in ortho position with respect to -CO-, R_2 is hydrogen; in this case the formula Ia) represents the acetylsalicylic acid residue;

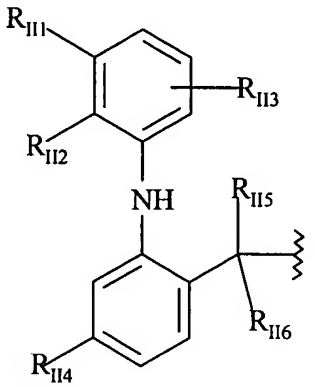
- R_1 = H R_2 = OH, preferably in ortho position with respect to -CO-, in this case the formula Ia) represents the salicylic acid residue;

in formula Ib) nI is an integer 0 or 1;

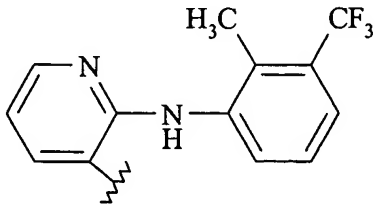
preferably in the compounds of formula Ib) $R_3 = CH_3$, nI = 0, T_1 = -CO-; in this case Ib) is the acetylsalicylsalicylic acid residue;

Group II)

IIa)



IIb)



wherein:

R_{II5} is H, C_1-C_3 linear or branched when possible alkyl;

R_{II6} has the same meaning as R_{II5}, or when R_{II5} is H it is benzyl;

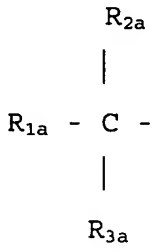
R_{II1}, R_{II2} and R_{II3} are independently hydrogen, C_1-C_6 linear or branched alkyl, or C_1-C_6 linear or branched alkoxy, or Cl, F, Br;

R_{II4} is R_{II1} or bromine;

the compounds are preferred wherein R_{II1}, R_{II4} are hydrogen and R_{II2} and R_{II3} are chlorine in ortho position with respect to NH; R_{II5} and R_{II6} are H, T_1 = -CO-, when the free valence is saturated with OH the precursor compound is known as diclofenac.

IIb) is the residue of the 2-[(2-methyl-3-(trifluoro methyl)phenyl]amino]-3-pyridincarboxylic] acid when T_1 =

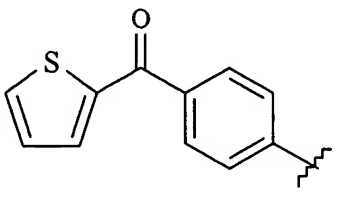
-CO- and the free valence is saturated with OH the compound is known as flunixin;



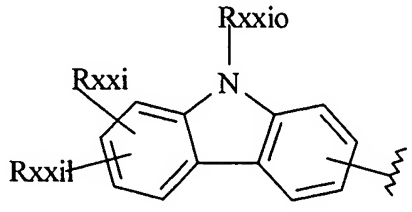
wherein:

R_{2a} and R_{3a} are H, C_1-C_{12} linear or branched, substituted or not, alkyl or allyl, with the proviso that when one of the two is allyl the other is H; preferably R_{2a} and R_{3a}, equal or different, are H, C_1-C_4 alkyl;

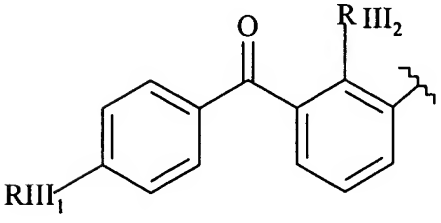
R_{1a} is selected from:

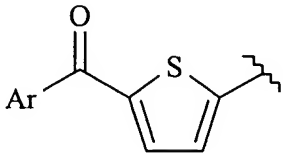


(II)

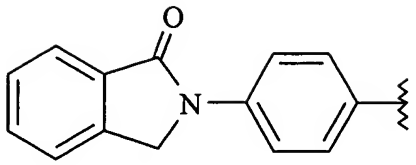


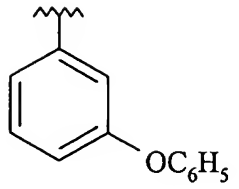
(XXI)



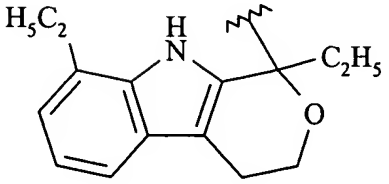


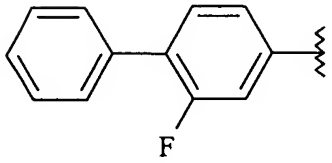
(IV) (XXXV)



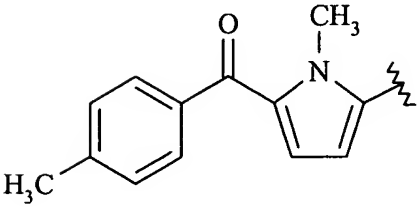


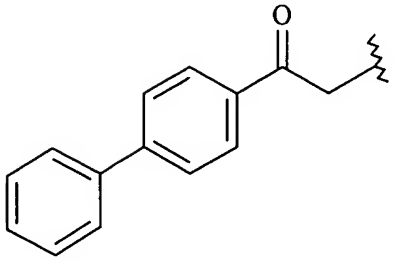
(VI) (VII)





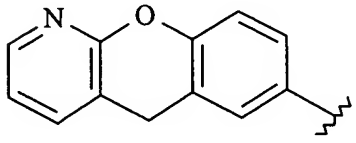
(VIII) (IX)

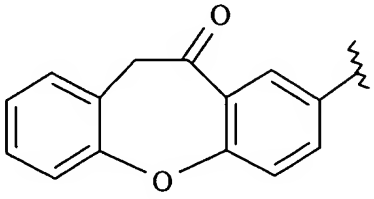




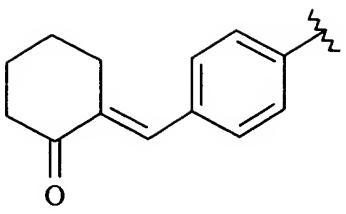
(X) (III)

IIID) R_{1a} corresponds to the following formulas:

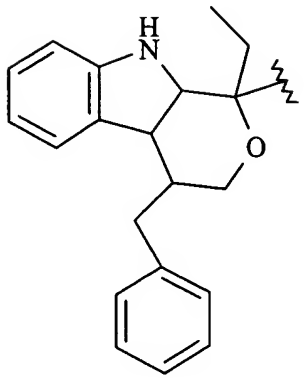




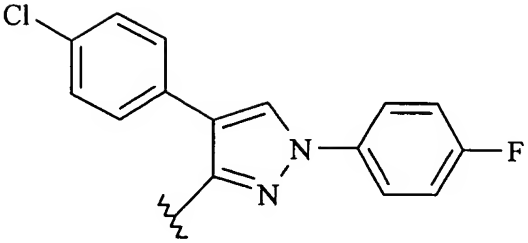
(IIIa) (XXX)



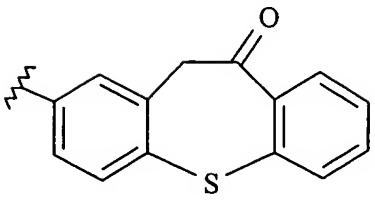
(XXXI)



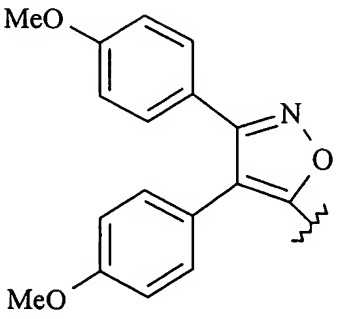
(XXXII)



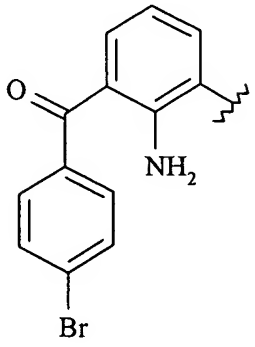
(XXXIII)



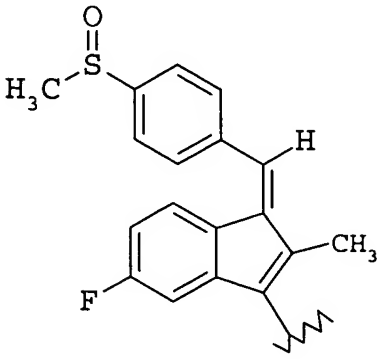
(XXXVI)



(XXXVII)



(XII)



(XXXX)

wherein the meanings are the following:

- when R_{1a} is as defined in formula (IV), Ketoprofen residue:

  R_{III1} is H, SR_{III3} wherein R_{III3} is C_1-C_4 linear or branched alkyl;

  R_{III2} is H, hydroxy;

  the compounds wherein R_{III1} and R_{III2} are H, R_{3a} is H, and R_{2a} is methyl, T_1 = -CO- are preferred;

- when R_{1a} is as defined in formula (XXI), carprofen residue:

  R_{xxio} is H, alkyl from 1 to 6 C atoms linear or branched, C_1-C_6 alkoxycarbonyl linked to a C_1-C_6 alkyl, C_1-C_6 carboxyalkyl, C_1-C_6 alkanoyl, optionally substituted with halogens, benzyl or halobenzyl, benzoyl or halobenzoyl;

  R_{xxi} is H, halogen, hydroxy, CN, C_1-C_6 alkyl containing or not containing OH groups, C_1-C_6 alkoxy, acetyl, benzyloxy, SR_{xxi2} wherein R_{xxi2} is C_1-C_6 alkyl; C_1-C_3 perfluoroalkyl; C_1-C_6 carboxyalkyl containing or not containing OH groups, NO_2, amino; sulphamoyl, di-alkyl sulphamoyl with C_1-C_6 alkyl, or difluoroalkylsulphonyl with C_1-C_3 alkyl;

  R_{xxi1} is halogen, CN, C_1-C_6 alkyl containing one or more OH groups, C_1-C_6 alkoxy, acetyl, acetamido, benzyloxy, SR_{III3} being R_{III3} as above, C_1-C_3 perfluoroalkyl, hydroxy, C_1-C_6 carboxyalkyl, NO_2, amino, C_1-C_6 mono- or di-alkyl-amino; sulphamoyl, C_1-C_6 di-alkyl-sulphamoyl, or di-fluoroalkylsulphamoyl as above; or R_{xxi} together with R_{xxi1} is a C_1-C_6 alkylen-dioxy;

  the compounds are preferred wherein R_{xxio} is H, the linking group is in position 2, R_{xxi} is H, R_{xxi1} is chlorine and is in para position with respect to the nitrogen;

  R_{3a} is H, R_{2a} is methyl and T_1 = -CO-;

- when R_{1a} is as defined in formula (XXXV) tiaprofenic acid residue:

  Ar is phenyl, hydroxyphenyl optionally mono- or polysubstituted with halogen, alkanoyl and C_1-C_6 alkoxy, C_1-C_6 trialkyl, preferably C_1-C_3, cyclopentyl, cyclohexyl, cycloheptyl, heteroaryl, preferably thienyl, furyl containing or not containing OH, pyridyl;

  the preferred compounds of (XXXV) are those wherein Ar is phenyl, R_{3a} is H, R_{2a} is methyl and T_1 = -CO-;

- when R_{1a} is as defined in formula (II), suprofen residue, R_{3a} is H, R_{2a} is methyl and T_1 = -CO-;

- when R_{1a} is as defined in formula (VI), R is the residue of indoprofen when T_1 = -CO-, R_{2a} = H and $R_{3a} = CH_3$; of indobufen when R_{2a} is equal to H and $R_{3a} = C_2H_5$; T_1 = -CO-;

- when R_{1a} is as defined in formula (VIII), R is the etodolac residue when $R_{2a} = R_{3a}$ = H and T_1 = -CO-;

- when R_{1a} is as defined in formula (VII), R is the fenoprofen residue when R_{3a} = H, $R_{2a} = CH_3$ and T_1 = -CO-;

- when R_{1a} is as defined in formula (III), R is the fenbufen residue when $R_{2a} = R_{3a}$ = H and T_1 = -CO-;

- when R_{1a} is as defined in formula (IX), R is the flurbiprofen residue when R_{3a} = H, $R_{2a} = CH_3$, T_1 = -CO-;

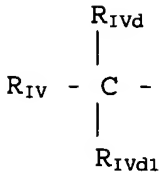
- when R_{1a} is as defined in formula (X) R is the tolmetin residue when $R_{2a} = R_{3a}$ = H, T_1 = -CO-.

In group IIID) R_{1a} corresponds to the following formulas:

- IIIa), when R_{2a} = H and $R_{3a} = CH_3$ the pranoprofen residue is obtained: α-methyl-5H-[1]benzopyran-[2,3-b]pyridin-7-acetic acid; in the preferred compound R_{2a} = H, $R_{3a} = CH_3$, T_1 = -CO- and in the precursor the free valence is saturated with OH;

- (XXX), when R_{2a} = H and R_{3a} = CH_3 the bermoprofen residue is obtained: dibenz[b,f]oxepin-2-acetic acid; in the preferred compound R_{2a} = H, R_{3a} = CH_3, T_1 = -CO-;
- (XXXI), when R_{2a} = H and R_{3a} = CH_3, R is the radical of the compound CS-670: 2-[4-(2-oxo-1-cyclohexyliden methyl) phenyl]propionic acid; the preferred compound has R_{2a} = H, R_{3a} = CH_3, T_1 = -CO-;
- (XXXII), when R_{2a} = R_{3a} = H, the pemedolac residue is obtained; when R_{2a} = R_{3a} = H T_1 = -CO-;
- (XXXIII), when R_{2a} = R_{3a} = H, the pirazolac residue is obtained: 4-(4-chlorophenyl)-1-(4-fluorophenyl)-3-pyrazol acid derivatives;
  the preferred compounds have R_{2a} = R_{3a} = H, T_1= -CO-;
- (XXXVI), when R_{2a} = H, R_{3a} = CH_3 the zaltoprofen residue is obtained; when the residue is saturated with an hydroxyl or aminic group, or with the carboxylic function the compounds are known as dibenzotiepin derivatives; in the preferred compounds R_{2a} = H, R_{3a} = CH_3, T_1 = -CO-;
- (XXXVII), when R_{2a} = R_{3a} = H the mofezolac residue is obtained: 3,4-di(p-methoxyphenyl)isoxazol-5-acetic acid when the residue is CH_2-COOH; in the preferred compounds R_{2a} = R_{3a} = H, T_1 = -CO-;
- (XII), when R_{2a} = R_{3a} = H the bromfenac residue is obtained: 2-amino-3-(4-bromobenzoyl)benzeneacetic acid; the preferred compounds have T_1 = -CO-, R_{2a} = R_{3a} = H;
- (XXXX) when R_{2a} = R_{3a} = H the sulindac residue is obtained: (Z)-5-fluoro-2-methyl-1-[[4-(methyl sulphinyl) –phenyl]methylene]-1H-inden-3-acetic aid; the preferred compounds have T_1 = -CO-, R_{2a} = R_{3a} = H;

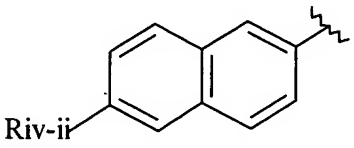
in Group IV) R is,



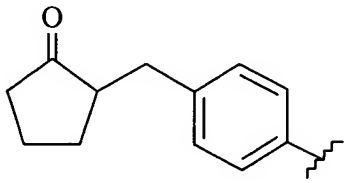
wherein:

R_{IVd} and R_{IVd1} are at least one H and the other an alkyl from C_1 to C_6 linear or branched, preferably C_1-C_2, or difluoroalkyl with C_1-C_6 alkyl, C_1 preferred, or R_{IVd} and R_{IVd1} form together a methylene group;

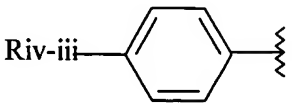
R_{IV} has the following meaning;



(IIB)



(XB)



(IIIB)

wherein the compounds of group IV) have the following meanings:

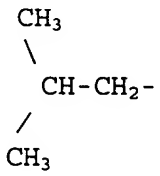
- in formula (IIB):

  $R_{IV\text{-}ii}$ is C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_7 alkoxymethyl, C_1-C_3 trifluoroalkyl, vinyl, ethynyl, halogen, C_1-C_6 alkoxy, difluoroalkoxy with C_1-C_7 alkyl, C_1-C_7 alkoxymethyloxy, alkylthiomethyloxy with C_1-C_7 alkyl, alkyl methylthio with C_1-C_7 alkyl, cyano, difluoromethylthio, phenyl- or phenylalkyl substituted with the C_1-C_8 alkyl; preferably $R_{iV\text{-}ii}$ is CH_3O-, R_{IVd} is H and R_{IVd1} is CH_3, and is known as naproxene residue; T_1 = -CO-;

- in formula (XB), of which the loxoprofen residue has been indicated, the compounds wherein R_{IVd} is H and R_{IVd1} is CH_3, T_1 = -CO- are preferred;
- in formula (IIIB):

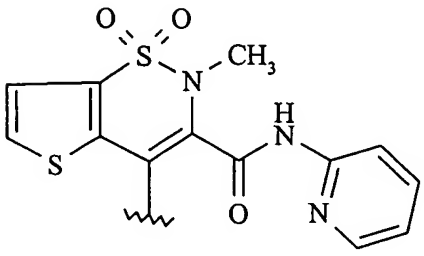
  $R_{iV\text{-}iii}$ is a C_2-C_5 branched or not branched alkyl, C_2 and C_3 alkyloxy, allyloxy, phenoxy, phenylthio, cycloalkyl from 5 to 7 C atoms, optionally substituted in position 1 by a C_1-C_2 alkyl;

  the compound is preferred wherein $R_{iV\text{-}iii}$ is

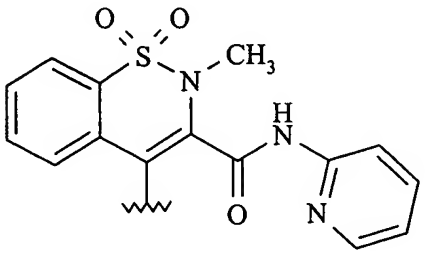


  and R_{IVd} = H, R_{IVd1} is CH_3, compound known as ibuprofen residue, T_1 = -CO-;

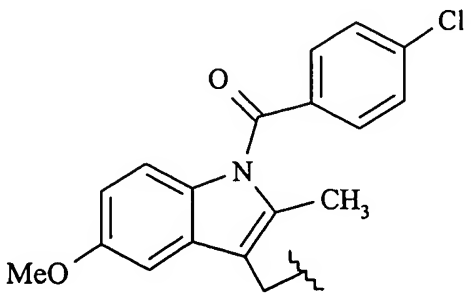
Group V)



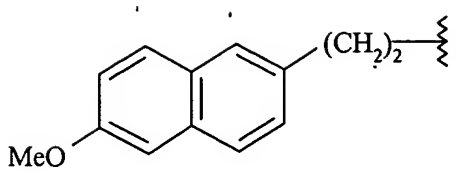
(VIIC)



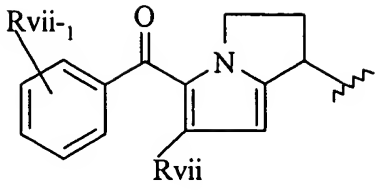
(IXC)



(IVC)

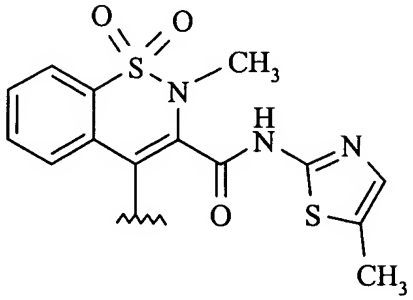


(IIIC)

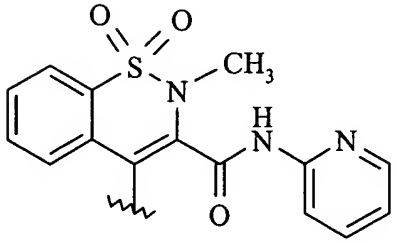


(IIC)

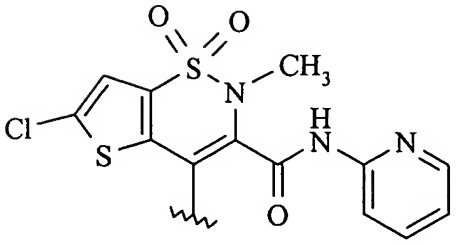
Group VE)



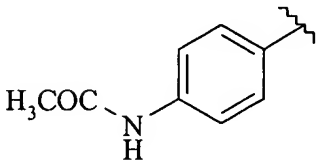
(XC)



(XI)



(XIII)



(XXXXV)

In group V), the compounds have the following meanings:

- when R is the formula (IIC),

  R_{Vii} is H or a C_1-C_4 linear or branched alkyl;

  R_{Vii-1} is R_{Vii}, or C_1-C_4 linear or branched alkoxy; Cl, F, Br; the position of R_{Vii-1} being ortho, or meta, or para;

  the Ketorolac residue is preferred, wherein R_{Vii} and R_{Vii-1} are H, and T_1 = -CO-;

- when R is the formula (VIIC),

of which the tenoxicam residue has been indicated, T_1 = -O-;

- when R is the formula (IXC),

  wherein T_1 = -O-, the piroxicam residue has been indicated;

- when R is the formula (IIIC),

  wherein T_1 = -CO-, of which the nabumetone residue has been indicated;

- when R is the formula (IVC),

  wherein T_1 = -CO-, of which the indomethacin residue has been indicated;

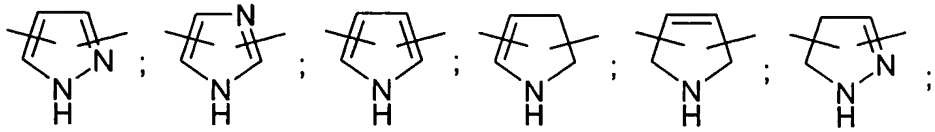
- when R is the formula (XC), the residue X is known as meloxicam; the preferred compounds are those in which T_1 = -CO-;

- when R is the formula (XI) the residue is known as ampiroxicam when the termination is $-CH(CH_3)OCOC_2H_5$; the preferred compounds have T_1 = -CO-;

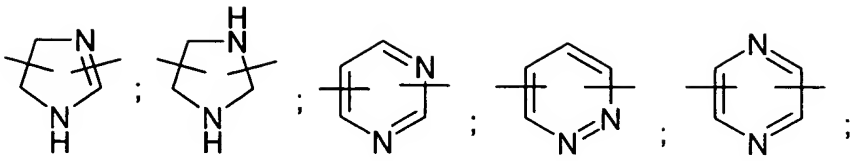
- when R is the formula (XIII) and the valence is saturated with H, the residue derives from lornoxicam; the preferred compounds have T_1 = -O-;

- when R is the formula (XXXXV), T_1 = -O- and the valence is saturated with H, the compound known as paracetamol is obtained.

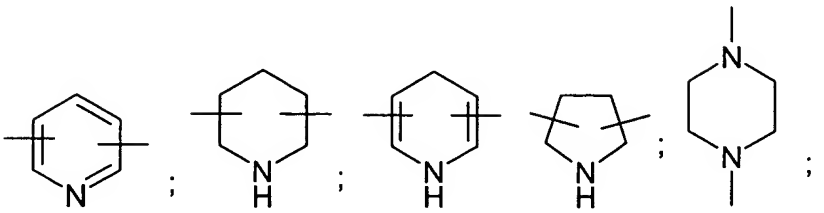
5. (Currently Amended) Use according to claims 1-4, wherein in the compounds of formula (I) Y^3 of formula (III^P) of C is selected from the following bivalent radicals:



(Y1) (Y2) (Y3) (Y4) (Y5) (Y6)



(Y7) (Y8) (Y9) (Y10) (Y11)



(Y12) (Y13) (Y14) (Y15) (Y16)

6. (Original) Use according to claim 5, wherein Y^3 is selected from the following: (Y12) with the two free valences in the ortho positions with respect to the nitrogen atom; (Y16) with the two valences linked to the two heteroatoms, Y1 (pyrazol) 3,5-disubstituted; Y16 is particularly preferred.

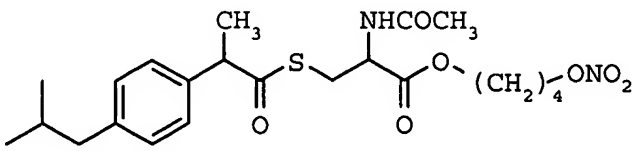
7. (Currently Amended) Use according to claims 1-~~6~~, wherein the following compounds are used:

2-acetyloxybenzoic acid 3-nitrooxymethyl phenyl ester (I^C);

2-fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 4-ni-trooxy butylester (II^C);

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-ni-trooxy butyl ester (III^C);

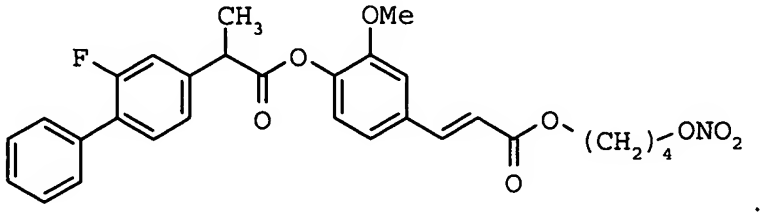
(S)-N-acetyl-[alpha-methyl-4-(2-methylpropyl)benzen-acetyl] cysteine 4-nitrooxybutylester having formula:



(IV^C)

4-nitrooxybutanoic acid 4-acetylaminophenylester (V^C);

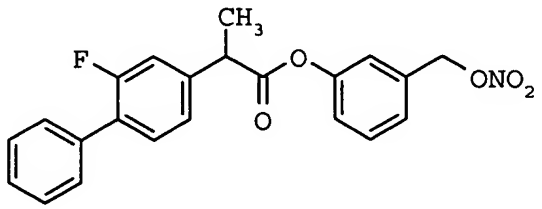
trans-3-[4-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyloxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy) butyl ester, having formula:



;

(VI^C)

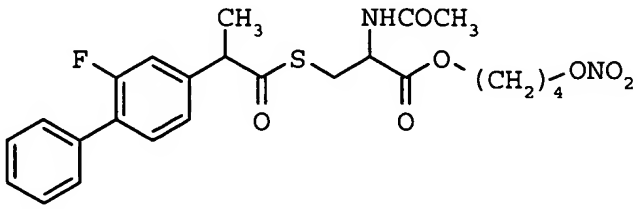
2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 3-(ni-trooxymethyl)phenyl ester having formula:



;

(VII^C)

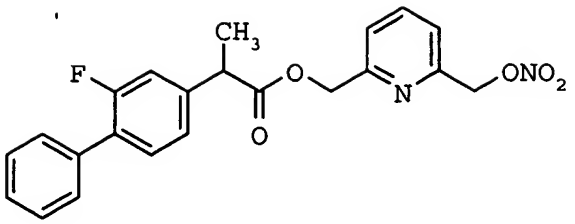
(S)-N-acetyl-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyl] cysteine 4-(nitrooxy)butyl ester having formula:



;

($VIII^C$)

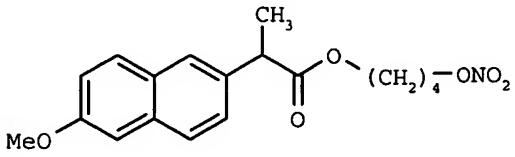
2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 6-(nitrooxy methyl)-2-methylpyridyl ester having formula



;

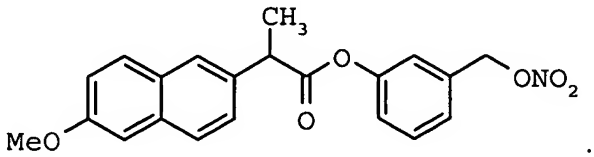
(XI^C)

(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 4-(nitrooxy)butyl ester having formula :



(X^C);

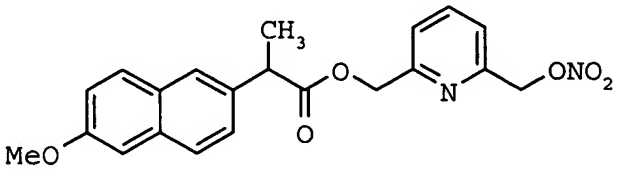
(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 3-(nitrooxymethyl)phenyl ester having formula:



;

(XI^B)

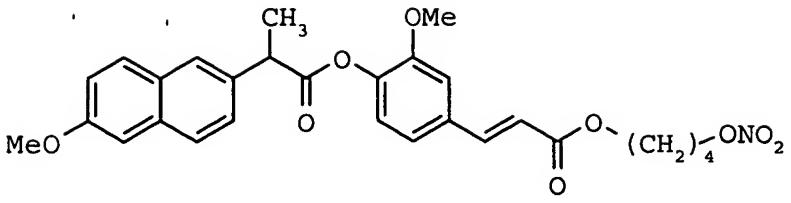
(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl ester having formula:



;

(XII^C)

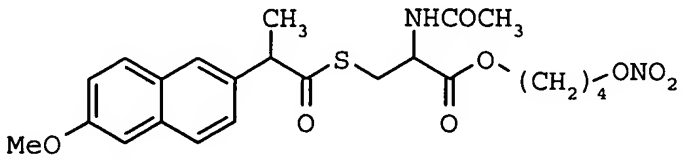
trans-3-[4-[6-methoxy-alpha-methyl-2-naphthalenacetyl oxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy)butyl ester having formula:



;

(XIII^C)

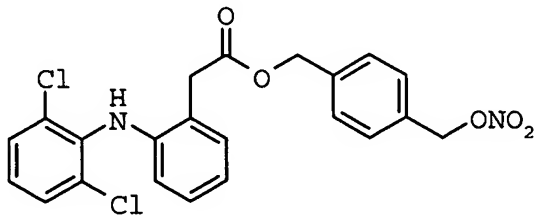
(S,S)-N-acetyl-S-(6-methoxy-alpha-methyl-2-naphthaleneacetyl) cysteine 4-(nitrooxy)butyl ester having formula:



;

(XIV^C)

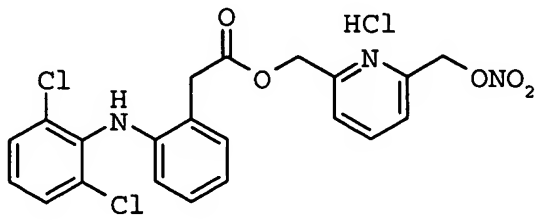
2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-(nitrooxy methyl)phenylmethyl ester having formula:



;

(XV^C)

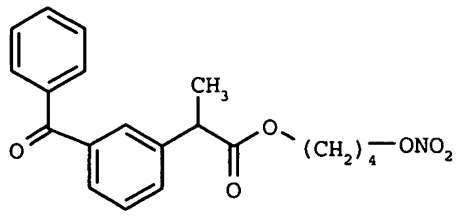
2-[(2,6-dichlorophenyl)amino]benzenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl hydrochloride ester having formula:



;

(XVI^C)

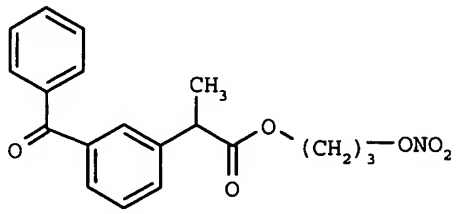
(S)-3-benzoyl-alpha-methyl-benzenacetic acid 4-(nitro oxybutyl) ester having formula:



;

(XVII^C)

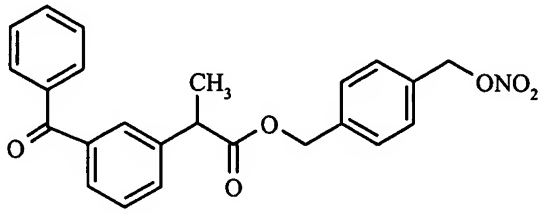
(S)-3-benzoyl-alpha-methyl-benzenacetic acid 3-(nitro oxypropyl) ester having formula:



;

(XVIII^C)

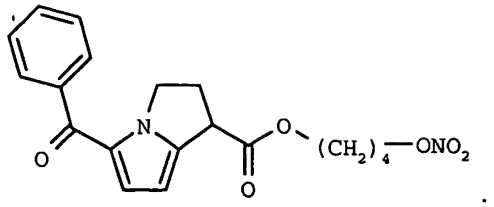
(S)-3-benzoyl-alpha-methyl-benzenacetic 4-(nitro oxymethyl) phenylmethyl ester having formula:



;

(XIX^C)

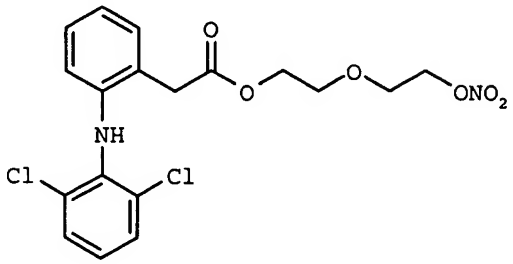
5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid 4-(nitrooxy)butyl ester having formula:



;

(XXI^C)

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 5 (nitro oxy)ethyloxyethyl ester having formula:



(XX^C)

1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid 3-(nitrooxymethyl)phenyl ester (XXI^C)

8. (Currently Amended) Use according to claims 1-~~7~~, wherein the compounds of formula (I) are administered in pharmaceutical formulations by oral, parenteral and topical administration.

9. (Currently Amended) Use according to claims 1-~~8~~ for the prevention of arthritis relapses.